SUPPLEMENTARY MATERIALS

TITLE: Safety of BNT162b2 COVID-19 vaccine in pregnancy: A systematic review

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Supplementary material

Table 1. Embase* search strategy

Concept Terms	#	Search string
Disease of interest	1	Coronavirus infection/
	2	Coronavirus disease 2019/
	3	("corona?vir*" or "COVID*" or "SARS Co?V?2").ti,ab.
	4	1 OR 2 OR 3
Intervention of interest	5	Vaccines/
	6	Immunization/
	7	(Vaccin* or immun* or inoculat*).ab,ti.
	8	5 OR 6 OR 7
	9	(mRNA or Pfizer or BioNTech or "BNT162b2" or Comirnaty or tozinameran or famtozinameran or riltozinameran or raxtozinameran or bretovameran or "COVID-19 mRNA vaccine encoding Wuhan-Hu-1 strain, Original, Original/Wuhan-Hu-1 strain; BA.4/BA.5; XBB.1.5; JN.1 and KP.2").ab,ti.
Combining concepts	10	8 and 9 [vaccines & Pfizer vaccine]
	11	4 and 10 [C-19 & (vaccines & Pfizer vaccine)]
Study design filter (RCTs)	12	(random* or factorial* or (crossover* or cross over*) or ((treble or triple or doubl* or singl*) adj blind*) or (assign* or allocat* or volunteer* or placebo*)).ti,ab. or crossover procedure/ or double blind procedure/ or single blind procedure/ or randomised controlled trial/ or clinical trial/ or controlled clinical trial/ or multicenter study/
Study design filter (Observational studies)	13	clinical study/ or case control study/ or family study/ or longitudinal study/ or retrospective study/ or prospective study/ or cohort analysis/ or follow-up/ or cohort*.ti,ab. or case control.ti,ab. or (cohort adj (study or studies or analys*)).ti,ab. or ((follow up or observational or uncontrolled or non randomi#ed or nonrandomi#ed or epidemiologic*) adj (study or studies)).ti,ab. or ((longitudinal or retrospective or prospective or cross sectional) and (study or studies or review or analys* or cohort*)).ti,ab.
Both study designs of interest	14	12 or 13
Combining concepts and study design filters	15	11 and 14
Removing irrelevant record types and using Ovid platform pre-print limit and date limit set to 2020 onwards	16	15 not (letter.pt. or letter/ or note.pt. or editorial.pt. or case report/ or case study/ or (letter or comment*).ti. or (animal/ not human/) or nonhuman/ or exp animal experiment/ or exp experimental animal/ or animal model/ or exp rodent/ or (rat or rats or mouse or mice).ti.)
Removing conference materials	17	16 not (exp conference paper/ or conference abstract/ or (conference adj (abstract or paper or review or proceeding)).pt

**Translated for use in Medline.*

Table 2. Eligibility criteria

Topic	Inclusion Criteria	Exclusion criteria
Population(s)	> Pregnant women and neonates	> Non-human studies
Intervention	> Receipt of at least one dose of Pfizer-BioNTech COVID-19 vaccine (BNT162b2, including adapted vaccines)	> No receipt of any dose of Pfizer-BioNTech COVID-19 vaccine (BNT162b2) > Receipt of heterologous regimen of Pfizer-BioNTech COVID-19 vaccine with a non-Pfizer-BioNTech COVID-19 vaccine > Mixed receipt of Pfizer-BioNTech and non-Pfizer-BioNTech COVID-19 vaccine within study population > Receipt of Pfizer-BioNTech COVID-19 vaccine co-administered with another vaccine (e.g., influenza)
Comparator	> Receipt of a differing number of doses of Pfizer-BioNTech COVID-19 vaccine (BNT162b2, including adapted vaccines) > No receipt of any COVID-19 vaccine (i.e., unvaccinated) in the control group or during a control period	> Receipt of a dose of any COVID-19 vaccine other than BioNTech (BNT162b2), including heterologous receipt of Pfizer-BioNTech COVID-19 vaccine
Outcomes	> Pregnancy-related adverse events, including but not limited to: o Spontaneous abortion or miscarriage o Preterm birth, stillbirth o Gestational diabetes or hypertension o Birth defects, congenital malformation o Foetal, neonatal, or maternal death o Antenatal or neonatal bleeding o Low birth weight, small for gestational age o Pre-eclampsia o Postpartum haemorrhage o Chorioamnionitis/funisitis	> Not reporting on outcomes of interest
Time	From 1st December 2020–current*	Prior to 1st December 2020

Study design	> Randomised controlled trials > Observational studies (cohort, case-control and pharmacovigilance) > Systematic literature reviews of COVID-19 vaccine safety and meta-analyses (for bibliography checks only)† > Data presented by national healthcare bodies: o US Centers for Disease Control and Prevention (e.g., Advisory Committee on Immunization Practices [ACIP]) o US Food and Drug Administration (e.g., Vaccines and Related Biological Products Advisory Committee [VRBPAC]) o UK MHRA o European Medicines Agency (EMA) o Brazilian Ministry of Health (National Immunization Program) o UAE Ministry of Health and Prevention (e.g., Emirates Drug Establishment) o Taiwan Centers for Disease Control o Singapore Ministry of Health (e.g., Health Sciences Authority) o South Africa National Department of Health (e.g., South African Health Products Regulatory Authority) o Argentina Ministry of Health (e.g., Administración Nacional de Medicamentos, Alimentos y Tecnología Médica) o Saudi Arabia Ministry of Health (Saudi Food and Drug Authority) o Mexico Ministry of Health (e.g., Comisión Federal para la Protección contra Riesgos Sanitarios)	> Non-peer-reviewed articles (not applicable to national healthcare body data) > Editorials > Case studies > Commentaries > Letters to journals > Abstracts (without full text available) > Non-systematic literature reviews > Study protocols > Conference minutes > Non-English publications‡

NA: not applicable.

**BNT162b2 was authorised for use from December 11th, 2020 onwards, therefore any relevant studies were published after this date.(55)*

†Pooled estimates from systematic literature reviews and meta-analyses with comparable research objectives were considered for extraction, while 3–5 of those identified with the most relevant but not directly comparable aims and reporting were subject to bibliographic checks.

‡Given the large proportion of relevant, high-quality literature anticipated for identification in the electronic database search in the English language, non-English publications were excluded at title and abstract screening level.

Table 3. Summary of included publication study design characteristics

Author, Year	Study design	Region – study location/setting	Data source (data collection period)	Observation period	Population of interest*
Goldshtein, 2022(20)	Retrospective cohort study	Israel – National registry	Pregnancy registry (March 2021 to September 2021)	Up to October 2021	16,697
Mansour, 2022(21)	Prospective cohort study	International – N/A	COVID-19 Vaccines International Pregnancy Exposure Registry (C-VIPER) (January 2021 to September 2021)	From vaccination to spontaneous abortion (SAB) or 20 weeks of gestation	1,576
Citu, 2022(56)	Retrospective cohort study	Romania – Obstetrics and Gynecology Clinic of the Timisoara Municipal Emergency Hospital	Electronic Medical Records (January 2020 to January 2022)	Pregnant women from January 2021; Non-pregnant women from January 2020	638
Kharbanda, 2023(24)	Retrospective case control study	US –8 Vaccine Safety Datalink sites†	Administrative and EHR data (November 2021 to June 2022)	28-42 days	72,749
Denoble, 2024(40)	Retrospective case control study	US –8 Vaccine Safety Datalink sites†	Electronic Medical Records (January 13, 2021, to February 28, 2022)	(Date that adjudicated stillbirths occurred within study period) February 14, 2021, to February 27 2022	254
Florentino, 2023(35)	Retrospective cohort study	Brazil – Live Birth Information System (SINASC), National Immunisation System (SI-PNI) and Mortality Information System (SIM)	Population-level health records (15 May 2021 to 23 October 2021)	September 2022	4,753
Wainstock, 2021(37)	Retrospective cohort study	Israel – Soroka University Medical Center computerised database	Electronic Medical Records (January 2021 to June 2021)	Until delivery	4,399
Peretz-Machluf, 2022(32)	Prospective cohort study	Israel – Tertiary medical center	MD Clone platform (March 2021 to July 2021)	N/A	3,240
Suseeladevi, 2024 (34)	Prospective cohort study	England – National linked dataset cohort	NHSE Secure Data Environment (December 2020 to October 2022)	Up to November 2022	27,945
Toussia-Cohen, 2022(36)	Prospective cohort study	Israel – N/R	Digital questionnaire (January 2021 to November 2021)	2-4 weeks following vaccination	162
Cahen-Peretz, 2023 (28)	Prospective cohort study	Israel – Hadassah Mt. Scopus Medical Center	Health records (April 2021 to January 2022)	N/R	213
Bookstein Peretz, 2021(19)	Prospective cohort study	Israel – Sheba Medical Center, Tel Hashomer, Israel	Digital questionnaire (January 2021 to February 2021)	2 weeks to 2 months following vaccination	390

Author, Year	Study design	Region – study location/setting	Data source (data collection period)	Observation period	Population of interest*
Kugelman, 2022(29)	Retrospective cohort study	Israel – Carmel Medical Center, Haifa, Israel	Electronic Medical Records (February 2021 to July 2021)	1–4 weeks after the second dose	930
Rottenstreich, 2022(33)	Retrospective cohort study	Israel – Two university-affiliated medical centers in Jerusalem‡	Electronic Medical Records (August 2021 to December 2021)	N/R	1,720
Rottenstreich, 2021(26)	Retrospective cohort study	Israel – Two university-affiliated medical centres in Jerusalem‡	Electronic Medical Records (January 2019 to April 2021)	N/R	712
Magnus, 2022(30)	Retrospective cohort study	Sweden and Norway – National registry	Pregnancy Register in Sweden and the Medical Birth Registry of Norway (January 2021 to January 2022)	Until end of pregnancy	20,424
Peretz-Machluf, 2024(31)	Cross-sectional study	Israel – Sheba Medical Center	Digital questionnaire (December 2020 to March 2021 and August 2021 to January 2022)	2-4 weeks after delivery	223
Rowe, 2025(38)	Retrospective cohort study	US – National database	Merative Marketscan Commercial Database & Multi-state Medicaid (August 2021 to September 2022)	Until end of pregnancy	78,052
Lacroix, 2025(25)	Prospective cohort study	France – National coverage	Digital questionnaire (November 2021 to December 2022)	Until end of pregnancy	771
Moro, 2022(46)	Pharmacovigilance cross-sectional study	US – National surveillance system	Vaccine Adverse Event Reporting System (December 2020 to October 2021)	N/A	1,831
Ahn, 2022(57)	Retrospective cohort study	Korea – National database	Korean National Health Service (November 2019 to July 2021)	Until end of pregnancy	205,263
Sut, 2023(27)	Prospective cohort study	Turkey – University Medical Faculty, Obstetrics and Gynaecology Clinic	Registration database of the Turkish Health Ministry (January 2022 to April 2022)	Until end of pregnancy	307
Covas, 2023(22)	Pharmacovigilance cross-sectional study	Brazil – National, State, Regional, Municipal and local level	Adverse event following immunization (AEFI) Surveillance Information System (April 2021 to August 2021)	N/A	572
Sadarangani, 2022(58)	Retrospective cohort study	Canada – Ontario, Quebec, British Columbia, Alberta, Nova Scotia, Yukon, and Prince Edward Island	Canadian National Vaccine Safety (CANVAS) Network surveys (December 2020 to November 2021)	7 days following vaccination dose	3,414

Author, Year	Study design	Region – study location/setting	Data source (data collection period)	Observation period	Population of interest*
Goldshtein, 2021(23)	Retrospective cohort study	Israel – National registry	Maccabi Healthcare Services Pregnancy registry (December 2020 to February 2021)	From the index date (first vaccine dose) to the earliest occurrence of an outcome of interest, leaving the fund, or EOS	7,530

AEFI: adverse event following immunization; C-VIPER: COVID-19 Vaccines International Pregnancy Exposure Registry; EHR: electronic health records; EMR: electronic medical records; EOS: end of study; MD: medical doctor; N/A: not applicable; N/R: not reported; NHSE: National Health Service England; SAB: spontaneous abortion; SIM: Mortality Information System; SINASC: Live Birth Information System; SI-PNI: National Immunisation System; VSD: Vaccine Safety Datalink

**, N (i.e., receiving Pfizer vaccine)*

† Kaiser Permanente, Washington, Northwest, Northern California, Southern California, and Colorado; Denver Health; HealthPartners; and Marshfield Clinic.

‡ Shaare Zedek Medical Center (SZMC) and the Bikur Holim Medical Center (BHMC)

Table 4. Pregnancy outcomes reported across included publications

Author, Year	SAB/ miscarriage	Preterm birth	Gestational diabetes/ hypertension	Birth defects, congenital malformation	Foetal (stillbirth), neonatal, or maternal death	Antenatal/ neonatal bleeding	Low birth weight/ small for gestational age	Pre-eclampsia	Postpartum haemorrhage	Chorioamnionitis/funisitis
Goldshtein, 2022(20)	–	X	–	–	X	–	X	–	–	–
Mansour, 2022(21)	X	–	–	–	–	–	–	–	–	–
Citu, 2022(56)	X	–	–	–	–	–	–	–	–	–
Kharbanda, 2023(24)	X	–	–	–	–	–	–	–	–	–
Denoble, 2024(40)	–	–	–	–	X	–	–	–	–	–
Florentino, 2023(35)	–	X	–	–	–	–	X	–	–	–
Wainstock, 2021(37)	–	–	X	–	–	–	X	–	X	–
Peretz-Machluf, 2022(32)	–	X	X	–	–	–	X	X	–	–
Suseeladevi, 2024 (34)	X	X	–	–	X	–	X	–	–	–
Toussia-Cohen, 2022(36)	–	X	–	–	–	X	–	–	–	–
Cahen-Peretz, 2023 (28)	–	X	X	–	–	–	X	–	–	–
Bookstein Peretz, 2021(19)	X	X	X	–	X	X	X	X	X	–
Kugelman, 2022(29)	–	X	X	–	X	–	X	–	–	–
Rottenstreich, 2022(33)	–	X	X	–	X	X	X	–	X	X
Rottenstreich, 2021(26)	–	X	X	–	X	X	X	–	X	X
Magnus, 2022(30)	–	X	–	–	–	–	X	–	–	–
Peretz-Machluf, 2024(31)	–	X	X	–	–	X	X	–	X	–
Rowe, 2025(38)	–	–	–	X	–	–	–	–	–	–
Lacroix, 2025(25)	X	–	–	X	X	–	–	–	–	–
Moro, 2022(46)	X	X	X	X	X	X	X	X	–	–
Ahn, 2022(57)	X	X	X	–	X	–	–	–	–	–

Author, Year	SAB/ miscarriage	Preterm birth	Gestational diabetes/ hypertension	Birth defects, congenital malformation	Foetal (stillbirth), neonatal, or maternal death	Antenatal/ neonatal bleeding	Low birth weight/ small for gestational age	Pre-eclampsia	Postpartum haemorrhage	Chorioamnionitis/funisitis
Sut, 2023(27)	X	X	X	X	X	–	–	X	–	–
Covas, 2023(22)	X	X	–	–	X	X	–	–	–	–
Sadarangani, 2022(58)	X	X	X	–	–	X	–	–	–	–
Goldshtein, 2021(23)	X	X	–	–	X	–	X	X	–	–

'X' reflects that the outcome was reported, '–' indicates the outcome was not reported.

SAB: spontaneous abortion

Table 5. Vaccination dose received in included publications

Author, Year	Type of vaccine (dose number/booster)	Unvaccinated	Vaccination not stratified by dose*	Dose 1	Dose 2	Dose 3
Goldshtein, 2022(20)	2 doses, no booster	7591 (31.3)	16697 (100)	–	–	–
Mansour, 2022(21)	2 doses, no booster	–	–	1574 (99.9)	1133 (72.1)	–
Citu, 2022(56)	First dose (assumed based on study period)	–	–	638 (100)	–	–
Kharbanda, 2023(24)	Third dose (booster)	–	–	–	–	NR (100)
Denoble, 2024(40)	≥1 dose	–	254 (100)	–	–	–
Florentino, 2023(35)	1, 2, or 3 doses	11170 (64.0)	–	1138 (18.0)	3081 (49.0)	534 (84)
Wainstock, 2021(37)	1 or 2 doses	3486 (79.)	–	155 (35.0)	758 (17.2)	–
Peretz-Machluf, 2022(32)	N/R	460 (12.4)	3240 (87.6)	–	–	–
Suseeladevi, 2024 (34)	One, two or booster doses	133405 (71.5)	27945 (57.2)	–	–	–
Toussia-Cohen, 2022(36)	2 doses and booster	–	–	162 (100)	162 (100)	84 (51.9)
Cahen-Peretz, 2023 (28)	2 doses and booster	–	–	213 (100)	213 (100)	86 (40.4)
Bookstein Peretz, 2021(19)	2 doses, no booster	–	–	390 (100)	390 (100)	–
Kugelman, 2022(29)	1 or 2 doses	–	–	930 (100)	879 (94.5)	–
Rottenstreich, 2022(33)	2 doses and booster	863 (33.4)	–	60 (2.3)	1720 (66.9)	626 (24.2)
Rottenstreich, 2021(26)	1 or 2 doses	1063 (59.9)	712 (40.1)	–	–	–
Magnus, 2022(30)	1 or 2 doses	129015 (81.9)	20424 (13.0)	–	–	–
Peretz-Machluf, 2024(31)	2 doses or booster	–	–	–	139 (62.3)	84 (37.7)
Rowe, 2025(38)	N/R	65327 (83.7)	41762	–	–	–
Lacroix, 2025(25)	1-3 doses	–	771 (82.2)	–	–	–
Moro, 2022(46)	N/R	–	1831 (52.9)	–	–	–
Ahn, 2022(57)	N/R	N/R (13.0)	205263 (4.9)	–	–	–
Sut, 2023(27)	N/R	55	307 (83.0)	–	–	–
Covas, 2023(22)	N/R	–	572 (23.0)	–	–	–
Sadarangani, 2022(58)	1 or 2 doses	339 (3.7)	–	3414 (37.7)	1892 (20.9)	–
Goldshtein, 2021(23)	1 dose	7530 (50.0)	–	7530 (100)	–	–

**E.g., 1 or 2 doses, ≥1 dose.*

N/R: not reported.

Table 6. NICE critical appraisal methodology checklist: cohort studies

Record information	Selection bias				Performance bias				Attrition bias				Detection bias						Overall assessment
Author, Year	1	2	3	Overall assessment	1	2	3	Overall assessment	1	2	3	Overall assessment	1	2	3	4	5	Overall assessment	
Goldshtein, 2022(20)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	X	Low risk	Low risk
Mansour, 2022(21)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	U	X	X	Low risk	Low risk
Citu, 2022(56)	X	X	–	High risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	X	Low risk	High risk
Florentino, 2023(35)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	X	Low risk	Low risk
Wainstock, 2021(37)	X	X	X	Low risk	–	–	–	High risk	X	X	X	Low risk	X	U	U	X	X	Unclear risk	Unclear risk
Peretz-Machluf, 2022(32)	X	X	X	Low risk	U	–	–	High risk	X	X	X	Low risk	X	X	X	X	–	Low risk	Low risk
Suseeladevi, 2024 (34)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	–	Low risk	Low risk
Toussia-Cohen, 2022(36)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	U	Low risk	Low risk
Cahen-Peretz, 2023 (28)	–	X	X	Unclear risk	U	–	–	Unclear risk	X	X	X	Low risk	X	X	X	U	U	Unclear risk	Unclear risk
Bookstein Peretz, 2021(19)	X	X	X	Unclear risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	U	Low risk	Unclear risk
Kugelman, 2022(29)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	–	Low risk	Low risk
Rottenstreich, 2022(33)	X	U	–	Unclear risk	U	–	–	High risk	X	X	X	Low risk	X	X	X	X	X	Low risk	Low risk
Rottenstreich, 2021(26)	X	X	X	Low risk	U	–	–	High risk	X	X	X	Low risk	X	X	X	X	–	Low risk	Low risk
Magnus, 2022(30)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	U	U	Low risk	Low risk
Peretz-Machluf, 2024(31)	X	X	X	Unclear risk	X	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	U	Low risk	Low risk
Rowe, 2025(38)	X	X	X	Low risk	X	–	–	Unclear risk	X	X	X	Low risk	X	U	U	X	–	Unclear risk	Unclear risk
Lacroix, 2025(25)	X	X	X	Low risk	X	–	–	Unclear risk	U	X	U	Unclear risk	X	U	X	X	–	Unclear risk	Unclear risk
Moro, 2022(46)	–	–	–	High risk	U	–	–	High risk	X	U	X	Low risk	X	X	X	X	–	Low risk	High risk
Ahn, 2022(57)	–	–	X	Unclear risk	X	–	–	Unclear risk	X	U	X	Low risk	X	U	X	X	–	Unclear risk	Unclear risk
Sut, 2023(27)	–	X	X	Low risk	U	–	–	High risk	X	X	X	Low risk	X	X	X	U	U	Unclear risk	Unclear risk
Covas, 2023(22)	–	–	–	High risk	–	–	–	Unclear risk	X	X	U	Low risk	–	–	–	–	–	High risk	High risk

Sadarangani, 2022(58)	X	–	–	High risk	X	–	–	Unclear risk	X	X	X	Low risk	–	U	U	X	–	High risk	High risk
Goldshtein, 2021(23)	X	X	X	Low risk	U	–	–	Unclear risk	X	X	X	Low risk	X	X	X	X	X	Low risk	Low risk

X = Yes; '–' = No; U = Unclear risk

Selection bias (systematic differences between the comparison groups):

1. *The method of allocation to treatment groups was unrelated to potential confounding factors (that is, the reason for participant allocation to treatment groups is not expected to affect the outcome[s] under study)*
2. *Attempts were made within the design or analysis to balance the comparison groups for potential confounders.*
3. *The groups were comparable at baseline, including all major confounding and prognostic factors.*

Performance bias (systematic differences between groups in the care provided, apart from the intervention under investigation):

1. *The comparison groups received the same care apart from the intervention(s) studied*
2. *Participants receiving care were kept 'blind' to treatment allocation*
3. *Individuals administering care were kept 'blind' to treatment allocation*

Attrition bias (systematic differences between the comparison groups with respect to loss of participants):

1. *All groups were followed up for an equal length of time (or analysis was adjusted to allow for differences in length of follow-up)*
2. *The groups were comparable for treatment completion (that is, there were no important or systematic differences between groups in terms of those who did not complete treatment)*
3. *The groups were comparable with respect to the availability of outcome data (that is, there were no important or systematic differences between groups in terms of those for whom outcome data were not available).*

Detection bias (bias in how outcomes are ascertained, diagnosed or verified):

1. *The study had an appropriate length of follow-up*
2. *The study used a precise definition of outcome*
3. *A valid and reliable method was used to determine the outcome*
4. *Investigators were kept 'blind' to participants' exposure to the intervention*
5. *Investigators were kept 'blind' to other important confounding and prognostic factors*

Table 7. NICE critical appraisal methodology checklist: case-control studies

Author, Year	The study addresses an appropriate and clearly focused question.	The cases and controls are taken from comparable populations	The same exclusion criteria are used for both cases and controls	Comparable participation rate for each group (cases and controls)?	Participants and non-participants are compared to establish their similarities or differences	Cases are clearly defined and differentiated from controls	It is clearly established that controls are not cases	Measures were taken to prevent knowledge of primary exposure from influencing case ascertainment	Exposure status is measured in a standard, valid and reliable way	The main potential confounders are identified and taken into account in the design and analysis	Have CIs been provided?	**Overall Assessment**
Kharbanda, 2023(24)	Well covered	Adequately addressed	Well covered	Adequately addressed	Poorly addressed	Adequately addressed	Well covered	Not applicable	Well covered	Adequately addressed	Yes	Low risk
Denoble, 2024(40)	Well covered	Well covered	Well covered	Adequately addressed	Poorly addressed	Adequately addressed	Well covered	Not applicable	Well covered	Adequately addressed	Yes	Low risk

CI: Confidence intervals

Table 8. Outcomes definitions matrix

Outcome	Common Definition Used Across Studies	Definition Variability Identified	Implications for Synthesis
Spontaneous abortion/miscarriage	Typically defined as pregnancy loss <20 weeks gestation (USA) or <22 weeks (Europe).	Some studies used clinical codes (ICD-10 O03), others relied on medical record confirmation. Timing thresholds differed (e.g., <20 weeks vs <24 weeks).	Variability in gestation.
Stillbirth/foetal death	Defined as ≥23 weeks of gestation	Timing thresholds ranged from ≥20 to ≥24 weeks	Variability in gestation.
Preterm birth	<37 weeks of gestation, very early/premature birth defined as <32 weeks.	All reporting studies consistently defined these thresholds.	None.
Small for gestational age (SGA)	Birthweight <10th percentile for gestational age	Despite majority of studies reporting on medical records, some studies did not provide definition or clinical codes. Outcome also described as intrauterine growth restriction.	Variability in threshold for SGA
Low birth weight (LBW)	No common definition applied.	Most studies reported birth weight without defining a 'low' threshold. Of those that did define, ≥2500–<4000g, and <10th percentile (referencing the International standards for foetal growth) (39)	Considerable variability in low birth weight.
Congenital malformations	One or more structural birth defect or chromosomal abnormalities (e.g., Down Syndrome).	Specific conditions included under umbrella terms varied between studies.	Variability in conditions included within grouped outcome terminology and composite measures.
Pre-eclampsia	'Pre-eclampsia'	Two studies based on standardised coded diagnosis (ICD and unspecified), rest authordefined based on medical records and one patient reported.	Likely minor variability between medical coding and patient reported.
Gestational diabetes and hypertension	Termed 'gestational diabetes mellitus', hypertensive disorders of pregnancy', and 'high blood pressure'.	One study specified ICD codes, most were based on medical record diagnoses without code specified. Two studies relied on patient questionnaires.	Variability in definition and terminology.
Postpartum haemorrhage	Estimated blood loss > 1000 mL	Author-defined, extent of bleeding unspecified and self-reported in one study.	Variability in extent of bleeding.
Antenatal bleeding	Vaginal bleeding	No specification of clinical codes, based on medical records and patient self-reporting.	Likely variability in extent of bleeding.
Neonatal bleeding	All grades of intracranial or intraventricular haemorrhage	No specification of clinical codes despite 'all grades' recognised, based on medical records and patient self-reporting.	None.
Chorioamnionitis	Diagnosis of one or more events	Based on medical code diagnosis, clinical code is not specified.	None.

Table 9. Operational Definitions and Effect Estimates for Pregnancy Outcomes Across Included Studies

Author, Year	Outcome	Operational definitions	Subpopulation	Effect Estimate	95% CI/Dispersion	p-Value	Direction of Effect
Goldshtein, 2022(20)	Preterm birth	Birth <37 weeks	Pre-IPTW	RR:1.1	0.95-1.27	N/A	No association
			Post-IPTW	RR: 0.95	0.83-1.1	N/A	No association
			Pre-IPTW First Trimester Vaccinated	RR: 1.15	0.91-1.46	N/A	No association
			Post-IPTW First Trimester Vaccinated	RR: 0.87	0.67-1.12	N/A	No association
			Pre-IPTW Vaccinated no maternal COVID-19 infection pre-birth	RR: 1.08	0.92-1.27	N/A	No association
			Post-IPTW Vaccinated no maternal COVID-19 infection pre-birth	RR: 0.94	0.81-1.10	N/A	No association
		Birth <32 weeks	Pre-IPTW	RR: 0.52	0.33-0.82	N/A	Lower risk among vaccine-exposed group
			Post-IPTW	RR: 0.45	0.29-0.70	N/A	Lower risk among vaccine-exposed group
			Pre-IPTW First Trimester Vaccinated	RR: 0.39	0.15-0.88	N/A	Lower risk among vaccine-exposed group
			Post-IPTW First Trimester Vaccinated	RR: 0.24	0.07-0.61	N/A	Lower risk among vaccine-exposed group
			Pre-IPTW Vaccinated no maternal COVID-19 infection pre-birth	RR: 0.57	0.35 to 0.96	N/A	Lower risk among vaccine-exposed group
			Post-IPTW Vaccinated no maternal COVID-19 infection pre-birth	RR: 0.58	0.35 to 0.98	N/A	Lower risk among vaccine-exposed group
		32-36 weeks	Pre-IPTW	RR: 1.18	1.02-1.38	N/A	Lower risk among vaccine non-exposed group
			Post-IPTW	RR: 1.03	0.89-1.20	N/A	No association
			Pre-IPTW First Trimester Vaccinated	RR: 1.3	1.01-1.67	N/A	Lower risk among vaccine non-exposed group
			Post-IPTW First Trimester Vaccinated	RR: 1.0	0.76-1.30	N/A	No association
			Pre-IPTW Vaccinated no maternal COVID-19 infection pre-birth	RR: 1.15	0.97 to 1.37	N/A	No association

Author, Year	Outcome	Operational definitions	Subpopulation	Effect Estimate	95% CI/Dispersion	p-Value	Direction of Effect
			Post-IPTW Vaccinated no maternal COVID-19 infection pre-birth	RR: 0.99	0.84 to 1.16	N/A	No association
Mansour, 2022(21)	Spontaneous abortion	N/A	Gestational age at vaccination: 6-<7 weeks	Cumulative risk: 2.3	0-6.1	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 7-<8 weeks	Cumulative risk: 3.4	0-6.1	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 8-<9 weeks	Cumulative risk: 5.7	1.4-8.5	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 9-<10 weeks	Cumulative risk: 6.8	2.6-10.3	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 10-<11 weeks	Cumulative risk: 7.7	4-12.3	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 11-<12 weeks	Cumulative risk: 8.8	4.4-12.8	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 12-<13 weeks	Cumulative risk: 9.6	4.8-13.3	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 13-<14 weeks	Cumulative risk: 9.6	4.9-13.6	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 14-<15 weeks	Cumulative risk: 10.3	5.4-14.1	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 15-<16 weeks	Cumulative risk: 10.3	5.5-14.2	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 16-<17 weeks	Cumulative risk: 10.4	5.5-14.2	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 17-<18 weeks	Cumulative risk: 10.4	5.5-14.2	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20

Author, Year	Outcome	Operational definitions	Subpopulation	Effect Estimate	95% CI/Dispersion	p-Value	Direction of Effect
		N/A	Gestational age at vaccination: 18-<19 weeks	Cumulative risk: 10.5	5.5-14.3	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
		N/A	Gestational age at vaccination: 19-<20 weeks	Cumulative risk: 10.9	5.9-14.7	N/A	Risk was higher in weeks 6 to 9 than weeks 10 to 20
Kharbanda, 2023(24)	Spontaneous abortion	N/A	Third Pfizer vaccination in 28-day window	Adjusted OR: 0.95	0.84-1.07	N/A	Not associated
			Any dose(s) of Pfizer vaccination in 28-day window	Adjusted OR: 0.93	0.83-1.05	N/A	Not associated
			Third Pfizer vaccination in 42-day window	Adjusted OR: 0.95	0.86-1.05	N/A	Not associated
			Any dose(s) of Pfizer vaccination in 42-day window	Adjusted OR: 0.94	0.85-1.03	N/A	Not associated
Denoble, 2024(40)	Foetal death	N/A	Total population	Adjusted OR: 1.00	0.69-1.43	N/A	Not associated
Florentino, 2023(35)	Preterm birth	Birth <37 weeks	Total population	HR: 1	0.88-1.11	N/A	Not associated
	Low birth rate	<2,500 grams	Total population	HR: 1.02	0.87-1.18	N/A	Not associated
	Small for gestational age	Birth weight <10th centile	Total population	HR: 1.1	0.95-1.27	N/A	Not associated
Wainstock, 2021(37)	Gestational diabetes	N/A	Total population	OR: 1.31	0.97-1.76	N/A	Not associated
	Small for gestational age	Birth weight <5th centile	Total population	OR: 0.75	0.49-1.15	N/A	Women who received the 2-dose vaccination delivered at slightly higher birth- weight
			One vaccination dose	OR: 0.66	0.4-1.07	N/A	
			Two vaccination doses	OR (vs unvaccinated): 1.21	vs unvaccinated: 0.56-2.64	N/A	
				OR (vs one dose): 1.82	vs one dose: 0.74-4.35	N/A	
	Pre-eclampsia	N/A	Total population	OR: 1.17	0.84-1.61	N/A	Not associated
			One vaccination dose	OR: 1.07	0.74-1.53	N/A	Not associated
			Two vaccination doses	OR (vs unvaccinated): 1.69	vs unvaccinated: 0.92-3.11	N/A	Not associated
				OR (vs one dose): 1.54	vs one dose: 0.79-3.02	N/A	Not associated

Author, Year	Outcome	Operational definitions	Subpopulation	Effect Estimate	95% CI/Dispersion	p-Value	Direction of Effect
	Postpartum haemorrhage	N/A	Total population	OR: 1.28	0.62-2.62	N/A	Not associated
Peretz-Machluf, 2022(32)	Preterm birth	Birth <37 weeks	Total population	OR: 0.94	0.62-1.44	N/A	Not associated
	Gestational hypertension	N/A	Total population	OR: 1.3	0.7-2.42	N/A	Not associated
	Small for gestational age	N/R	Total population	OR: 1.01	0.66-1.55	N/A	Not associated
Suseeladevi, 2024 (34)	Preterm birth	24 to <32 weeks	Total population	HR: 0.79	0.65-0.97	0.025	Lower risk among vaccine-exposed group
			Sensitivity analysis population	HR: 0.54	0.41-0.71	<0.0001	Lower risk among vaccine-exposed group
		32 to 36 weeks	Total population	HR: 0.93	0.87-0.99	0.016	Lower risk among vaccine-exposed group
			Sensitivity analysis population	HR: 1.03	0.94-1.12	0.57	Not associated
	Small for gestational age	Birth weight <10th centile	Total population (super pre-term)	HR: 0.85	0.53-1.34	0.48	Not associated
			Total population (pre-term)	HR: 0.97	0.73-1.30	0.85	Not associated
			Total population (normal age)	HR: 0.93	0.86-1.01	1.0	Not associated
			Sensitivity analysis population (super pre-term)	HR: 0.54	0.30-0.97	0.41	Lower risk among vaccine-exposed group
			Sensitivity analysis population (pre-term)	HR: 0.99	0.64-1.51	0.94	Not associated
			Sensitivity analysis population (normal age)	HR: 1.0	0.89-1.13	1.0	Not associated
Toussia-Cohen, 2022(36)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Cahen-Peretz, 2023 (28)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Bookstein Peretz, 2021(19)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Kugelman, 2022(29)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Author, Year	Outcome	Operational definitions	Subpopulation	Effect Estimate	95% CI/Dispersion	p-Value	Direction of Effect
Rottenstreich, 2022(33)	Preterm birth	Birth <37 weeks	Receiving booster dose	Adjusted OR (vs two doses): 0.82	0.73-0.93	<0.01	Lower risk among booster vaccinated group
				Adjusted OR (vs unvaccinated): 0.74	0.65-0.84	<0.01	Lower risk among vaccine-exposed group
	Gestational diabetes	N/A		Adjusted OR (vs two doses): 2.88	1.75-4.76	<0.01	Lower risk among primary series vaccinated group
				Adjusted OR (vs unvaccinated): 3.69	2.15-6.31	<0.01	Lower risk among unvaccinated group
	Low birth weight	N/R		Adjusted OR (vs two doses): 1.00	1.00	0.01	Not associated
				Adjusted OR (vs unvaccinated): 1.00	1.00	0.07	Not associated
Rottenstreich, 2021(26)	Spontaneous abortion	N/A	1 or 2 doses	Adjusted OR (vs unvaccinated): 1.05	0.78-1.40	0.77	Not associated
	Preterm birth	Birth <37 weeks		Adjusted OR (vs unvaccinated): 0.70	0.62-0.79	<0.01	Lower risk among vaccine-exposed group
	Gestational diabetes	N/A		Adjusted OR (vs unvaccinated):1.58	0.89-2.78	0.12	Not associated
	Gestational hypertension	N/A		Adjusted OR (vs unvaccinated): 2.13	0.79-5.73	0.13	Not associated
	Low birth weight	N/R		Adjusted OR (vs unvaccinated): 1.00	1.00	0.22	Not associated
Magnus, 2022(30)	Preterm birth	Birth <37 weeks	Total population	Adjusted HR:0.96	0.898-1.04	N/A	Not significantly associated
			Swedish population	Adjusted HR: 0.97	0.89, 1.06	N/A	Not significantly associated
			Norwegian population	Adjusted HR: 0.91	0.76, 1.10	N/A	Not significantly associated
	Small for gestational age	Birth weight <10th centile	Total population	Adjusted HR: 0.96	0.0.90, 1.03	N/A	Not significantly associated
			Swedish population	Adjusted HR: 1.04	0.90, 1.03	N/A	Not significantly associated
			Norwegian population	Adjusted HR: 0.96	0.96, 1.25	N/A	Not significantly associated
Peretz-Machluf, 2024(31)	Preterm birth	Birth <37 weeks	N/A	Adjusted OR: 0.57	0.086-3.84	0.567	No increased risk
	Gestational hypertension	N/A	N/A	Adjusted OR: 3.13	0.451-21.7	0.248	No increased risk
	Small for gestational age	Intrauterine growth restriction	N/A	Adjusted OR: 0.63	0.127-3.10	0.63	No increased risk
Rowe, 2025(38)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

Author, Year	Outcome	Operational definitions	Subpopulation	Effect Estimate	95% CI/Dispersion	p-Value	Direction of Effect
Lacroix, 2025(25)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Sut, 2023(27)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Covas, 2023(22)	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Goldshtein, 2021(23)	N/A	N/A	N/A	N/A	N/A	N/A	N/A

AEFI: adverse event following immunization; CI: confidence interval; HR: hazard ratio; IPTW: inverse probability of treatment weighting; N/A: not applicable; N/R: not reported; OR: odds ratio; RR: risk ratio

Table 10. PRISMA 2020 for Abstracts Checklist

Section and Topic	Item #	Checklist item	Reported (Yes/No)
TITLE			
Title	1	Identify the report as a systematic review.	Yes
BACKGROUND			
Objectives	2	Provide an explicit statement of the main objective(s) or question(s) the review addresses.	Yes
METHODS			
Eligibility criteria	3	Specify the inclusion and exclusion criteria for the review.	Yes
Information sources	4	Specify the information sources (e.g. databases, registers) used to identify studies and the date when each was last searched.	Yes
Risk of bias	5	Specify the methods used to assess risk of bias in the included studies.	Yes
Synthesis of results	6	Specify the methods used to present and synthesise results.	Yes
RESULTS			
Included studies	7	Give the total number of included studies and participants and summarise relevant characteristics of studies.	Yes
Synthesis of results	8	Present results for main outcomes, preferably indicating the number of included studies and participants for each. If meta-analysis was done, report the summary estimate and confidence/credible interval. If comparing groups, indicate the direction of the effect (i.e. which group is favoured).	Yes
DISCUSSION			
Limitations of evidence	9	Provide a brief summary of the limitations of the evidence included in the review (e.g. study risk of bias, inconsistency and imprecision).	Yes
Interpretation	10	Provide a general interpretation of the results and important implications.	Yes
OTHER			

Section and Topic	Item #	Checklist item	Reported (Yes/No)
Funding	11	Specify the primary source of funding for the review.	Yes
Registration	12	Provide the register name and registration number.	Yes

Table 11. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Page 1
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Page 2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Page 3
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Page 4
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 5
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 4-5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 4-5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 6
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 6

Section and Topic	Item #	Checklist item	Location where item is reported
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	Page 6
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Page 6
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Page 6
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	Page 6
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	Page 6
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Page 6
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Page 6
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 7
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 7
Study characteristics	17	Cite each included study and present its characteristics.	Supplementary materials 6-8
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	Supplementary materials pages 6-8
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Supplementary materials pages 12-13
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Supplementary materials pages 15-20
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Page 11-12
	23b	Discuss any limitations of the evidence included in the review.	Page 13
	23c	Discuss any limitations of the review processes used.	Page 13
	23d	Discuss implications of the results for practice, policy, and future research.	Page 14
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Page 15
Competing interests	26	Declare any competing interests of review authors.	Page 15
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Page 15